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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/965,131	09/26/2001	Maureen Angela Chung	WII-014CP	1805

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EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1632	14

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/965,131	Chung
Examiner	**Art Unit**
Anne Marie Wehbé	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 13, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-36* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response to the restriction requirement received on 1/13/03 has been entered. Please note that the examiner of record for the instant application has changed, see page 7. Claims 1-36 are pending in the instant application. Applicant's election with traverse of the subject matter of Group I, claims 1-19, and 25-36 is acknowledged. In view of applicant's arguments, the restriction requirement has been withdrawn. Claims 1-36 are currently under examination. An action on the merits follows.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 20 recites an E. coli-BCG shuttle plasmid which, when expressed in a mycobacterium, results in specificity for a tumor antigen. It is unclear what is meant by "specificity for a tumor antigen". The plasmid recited comprises DNA encoding a cytokine and DNA encoding a tumor antigen. A recombinant mycobacterium containing the recited plasmid

would express the tumor antigen and the cytokine. It is unclear how this plasmid or mycobacterium could have a "specificity" for the tumor antigen itself. The specification discloses the generation of tumor antigen specific immune responses. In this situation, the immune effectors stimulated by the mycobacterium have the specificity for the tumor antigen, not the mycobacterium or plasmid itself. Thus, based on the applicant's use of the term "specificity", the metes and bounds of the claim cannot be determined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scholl et al. (Sept. 1, 2000) J. Immunother., Vol. 23(5), 570-580 in view of US Patent. No. 5,776,465 (1998), hereafter referred to as O'Donnell '465, or US Patent NO. 5,591,632 (1997), hereafter referred to as O'Donnell '632. The applicant claims recombinant mycobacterium BCG comprising a plasmid which encodes a cytokine operatively linked to the BCG alpha antigen signal sequence under transcriptional control of a promoter and a tumor antigen under transcriptional control of a promoter. The applicant further claims method of stimulating an anti-tumor immune response, and methods of treating or preventing cancer comprising administering said recombinant BCG. In addition, the applicant claims said recombinant BCG wherein the cytokine is IL-2, wherein the tumor antigen is MUC-1, and wherein the first and second promoters are hsp60 or hsp70. The applicant also claims wherein either the cytokine or antigen further comprise an HA epitope tag.

Scholl et al. teach the generation of therapeutic anti-tumor immune responses and the treatment or prevention of breast cancer comprising the administration of a recombinant vaccine encoding MUC-1 and IL-2 (Scholl et al., page 570, page 571, Figure 1, page 575-576, Figures 3-4).

Scholl et al. differs from the instant invention in that Scholl et al. teaches the use of a recombinant vaccinia virus as the vaccine vector. O'Donnell '465 or '632 supplements Scholl et al. by teaching recombinant BCG which can be used to generate therapeutic immune responses *in vivo*. In particular, O'Donnell '465 or '632 teaches recombinant BCG which comprise a BCG shuttle plasmid encoding at least one antigen or cytokine under transcriptional control of either

the hsp60 or hsp70 promoters (O'Donnell '465, columns 13-20, and Figures 1A, 4A, and 4B, and O'Donnell '632, columns 11-20, columns 23-26, and Figures 1A,4A, and 4B). In particular, O'Donnell teaches a cytokine, IL-2, operatively linked to an HA epitope tag and the BCG alpha antigen signal sequence (O'Donnell '465, columns 17-18, and Figures 4A and 4B, and O'Donnell '632, Figures 4A, 4B, and columns 23-26, claims 1-28). O'Donnell teaches that the HA epitope tag is useful for detecting the expression of the encoded genes (O'Donnell '465, column 18, O'Donnell '632, column 18). O'Donnell et al. further teaches that immunization of mice with a BCG encoding an antigen results in the generation of antigen specific CTL and antibody responses, and that the immunization of mice with BCG encoding IL-2 results in enhanced stimulation over immunization with BCG without IL-2 (O'Donnell '465, column 20, and columns 23-24, claims 1-4), and O'Donnell '632, column 20, and columns 23-26, claims 1-28). O'Donnell et al. further teaches the construction of a multivalent recombinant BCG vaccine which encodes both an antigen **and** a cytokine, particularly IL-2 (O'Donnell '465, columns 10-11, bridging paragraph, O'Donnell '632, column 11). O'Donnell teaches that administration of the multivalent BCG vaccine would result in stimulation of an immune response to an antigen as well as a more potent stimulation of T cells and macrophages (O'Donnell '465, column11, lines 2-4, and O'Donnell '632, column 11, lines 23-25). O'Donnell also provides motivation for using the disclosed BCG vaccines for treating cancer (O'Donnell '465, column 11, lines 12-18, and O'Donnell '632, column 11, lines 33-39).

O'Donnell et al. further provides motivation for substituting a multivalent BCG for the vaccinia virus taught by Scholl et al. by teaching that BCG vaccines have important advantages over presently-available vaccines. Specifically, O'Donnell teaches that the adjuvant properties of mycobacteria are the best currently known, that BCG can be used repeatedly, and that BCG immunization results in long-term T cell memory responses and secondary antibody responses (O'Donnell '465, columns 2-3, bridging paragraph, and lines 1-37, and O'Donnell '632, column 3, lines 16-57). Thus, based on the advantages of BCG vaccines over other known vaccine systems, and the teachings of O'Donnell that BCG can be engineered to express an antigen and a cytokine to treat cancer, it would have been *prima facie* obvious to the skilled artisan to substitute a recombinant BCG for vaccinia virus in the method of treating cancer taught by Scholl et al. The skilled artisan would further have had a reasonable expectation of success in modifying the BCG-IL-2 vector taught by O'Donnell et al. to include a MUC-1 antigen sequence operatively linked to the hsp70 promoter in view of the detailed teachings in O-Donnell et al. for making recombinant BCG encoding antigens and cytokines. In addition, the skilled artisan would have had a reasonable expectation of success in generating therapeutic anti-MUC-1 immune responses using a recombinant BCG which expresses MUC-1 and IL-2 based on the proven efficacy of combined MUC-1 and IL-2 cancer therapy as taught by Scholl, and the successful use of BCG vaccines to generate antigen-specific immune responses taught by O'Donnell, '465 or '632.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Fri from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D.
PRIMARY EXAMINER